EXHIBIT Q

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Degradation of polypropylene in the human eye: A sem-study

W.L. JONGEBLOED[1] and J.F.G. WORST[2]

[1] Centre for Medical Electron Microscopy, University of Groningen, 69/2 Oostersingel, 9713 EZ Groningen; [2] Eye Physician and Surgeon, 11 Julianalaan, Haren, The Netherlands

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Abstract. A polypropylene surgical suture, which had served as fixation suture for an IOL for a period of 6.5 years, was removed from the eye of a Dutch patient because it had broken at one end and thus formed a potential risk for a corneal touch syndrome. After careful rinsing in 50% ethanol, to remove adhering debris, it was prepared for SEM.

A virgin piece of polypropylene material from a surgical package underwent the same preparative procedure.

The fixation suture showed cracks perpendicular to the longitudinal axis of the suture; part of the surface layer was nearly detached or completely missing; while the diameter of the suture was decreased towards both ends by over 50% in comparison with the original diameter.The exposed subsurface layer showed a fibrillar structure. The degradation phenomena are considered to be caused by the enzymatic action of tissue-fluids.

Virgin material did not show any of the phenomena observed on the fixation suture under consideration.

Introduction

Polypropylene material has been used in the past and is still used for surgical sutures and for lens haptics in the human eye as an alternative to nylon and supramid.

The biocompatibility of these materials has been questioned by several authors: Jongebloed et al. (1986), Apple et al. (1984), Drews (1983a, 1983b) and many others.

There is sufficient evidence that these materials can degrade after having been in the human eye for a period of several years. There are strong indications that enzymatic activity of the tissue fluid in the human eye is the cause of the surface changes on polypropylene, as well as on nylon and supramid, as has already been established.

Artifacts due to drying or irradiation damage in the SEM can be ruled out as possible causes. On the other hand the influence of sterilizing agents could make the polypropylene material more vulnerable to enzymatic disintegration, and so could UV-light. Moreover, the degradation effects observed in polypropylene are often associated with inflammatory con-

* The work was carried out at the Centre for Medical Electron Microscopy.

ditions in the human eye. It is probable that the drying procedure, necessary for SEM-observations, enhances the effect of peeling-off of part of the surface of the material.

The polypropylene suture under investigation had resided in the human eye for 6.5 years as fixation suture for an IOL and had to be removed because it had partially disintegrated and formed a potential risk for corneal touch.

Materials and methods

A polypropylene suture of 6.5 mm length, which had served as a fixation suture for an IOL during 6.5 years, was removed from the eye of a Dutch patient because it had partially disintegrated.

To remove adhering debris the suture was carefully washed with 50% ethanol, dried in air, placed on double adhesive tape and sputtercoated with Au (appr. 15 nm).

A virgin piece of polypropylene was used as a control and received the same preparation procedure as the suture under investigation. Both samples were examined with a JEOL SEM, type 35C, operated at 15 kV.

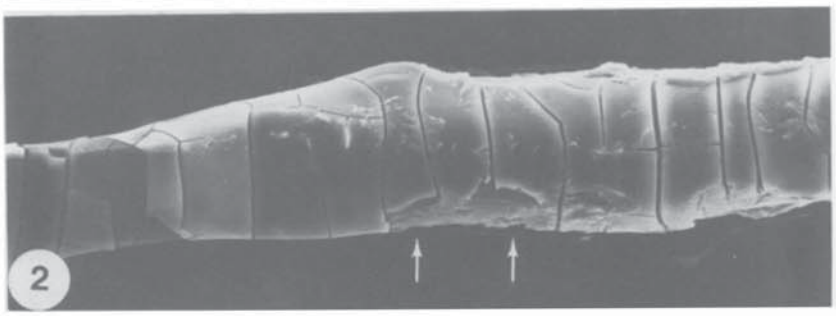
Results

The polypropylene suture which had been in the human eye for $6\frac{1}{2}$ years as fixation suture for an IOL is shown at low magnification in Figure 1. The left end (l) and the right end (r) of the suture show a considerable decrease in suture diameter in comparison with the central part (c). The right end had spontaneously broken, while the left end was cut off to free it from the surrounding tissue.

Figures 2 and 3 represent parts of the left side of the suture, cracks perpendicular to the longitudinal axis of the suture are visible. Lumps of the surface layer are nearly detached or are already missing (arrows). Note also the irregularity of the diameter of the suture in both pictures.

Figures 4 and 5 also represent parts of the left side of the used suture of Figure 1. The cracking of the surface layer is very obvious in Figure 4; almost the complete surface layer has been split off from the underlying layer. The outer surface of the lumps is covered with a thin layer of probably organic material with a slightly granular appearance (Figure 4). Closer to the central part of the suture (the part which was not in direct contact with the tissue) the disintegration of the polypropylene appears to be considerably less extensive. Figure 5 represents a part of the suture left of the centre, the cracks in the surface layer are already present and the diameter decreases towards the left side of the suture.

Figures 6 and 7 represent details of Figures 3 and 4 respectively, showing the subsurface layer after splitting off of the lumps of the surface layer. The subsurface layer shows a fibrillar character and the splitting off



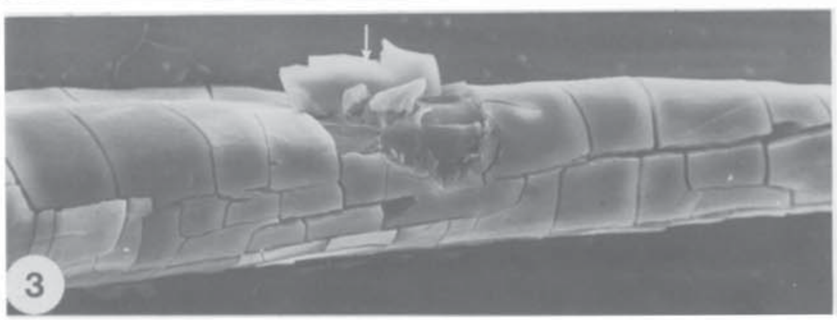


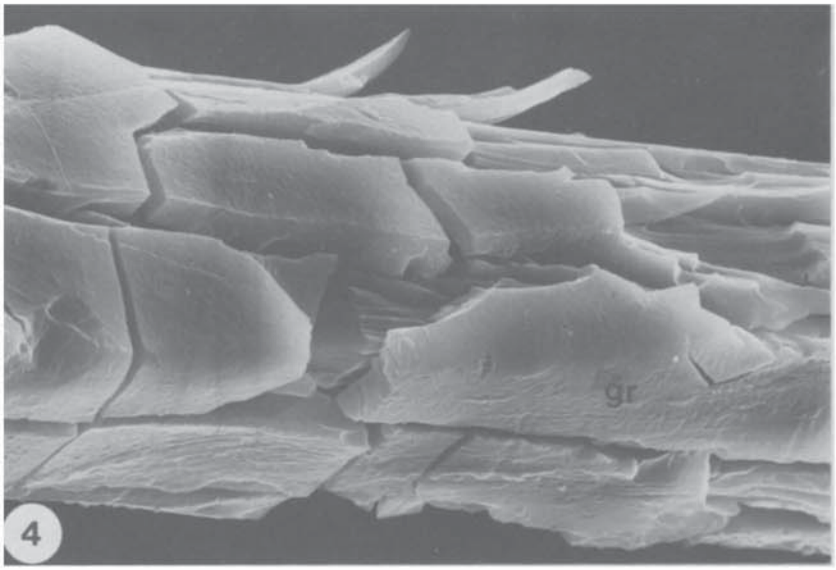
Figure 1. Polypropylene suture which remained for $6\frac{1}{2}$ years in a human eye as a fixation suture; l = cut-off end, diameter appr. 100 μm; r = spontaneously broken off end, diameter appr. 60 μm; c = central part, not in direct contact with tissue, diameter 200 μm. Magn. 20 ×.

Figure 2. Part of left side of suture of Figure 1, showing cracks in surface layer and missing part of surface layer (arrows); note irregular diameter. Magn. 225 ×.

Figure 3. Part of left side of suture of Figure 1, showing cracks in surface layer and nearly detached lump of surface layer (arrow); note somewhat twisted shape of suture. Magn. 325 ×.

of the surface layer is clearly observable. The outside of the lumps of the surface layer is covered with a thin layer of organic material with a slightly granular appearance.

Figure 8 represents the central part of the suture, some cracks in the surface are already visible and some deposition of material. The diameter



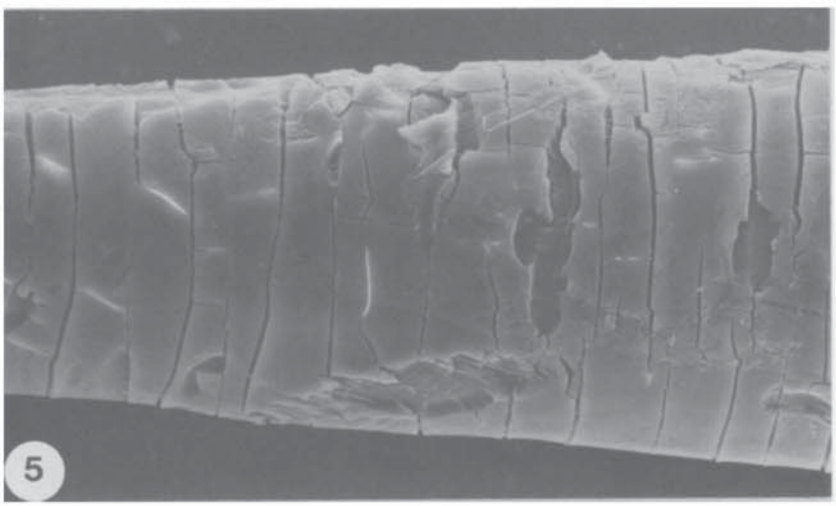
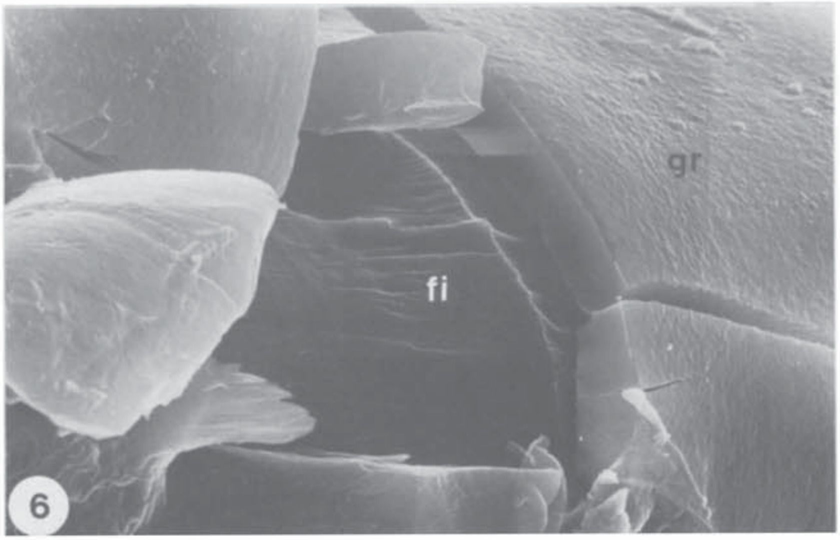


Figure 4. Part of left side of suture of Figure 1 showing completely disintegrated surface layer, large lumps nearly detached. Magn. 1000 ×.

Figure 5. Part of left side of suture of Figure 1, close to central part of suture. Surface less attacked; note decreasing diameter towards left side. Magn. 300 ×.

still has its original value of 200 μm. Figures 9–13 represent sections of the right side of the suture of Figure 1.

Figure 9 shows the irregular diameter and the splitting off of parts of the surface layer, at low magnification.



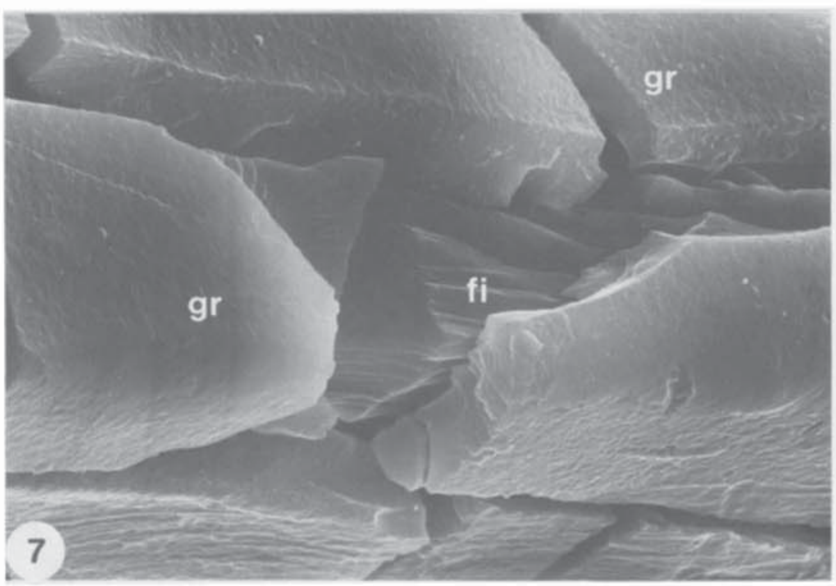


Figure 6. Detail of Figure 3 showing subsurface layer with fibrillar character (fi); note thin organic deposit with granular character (gr) on outside of lumps of surface layer. Magn. 2000 ×.

Figure 7. Detail of Figure 4 showing splitting of surface layer from underlying layer with fibrillar appearance (fi); lumps covered with somewhat granular material (gr). Magn. 2000 ×.

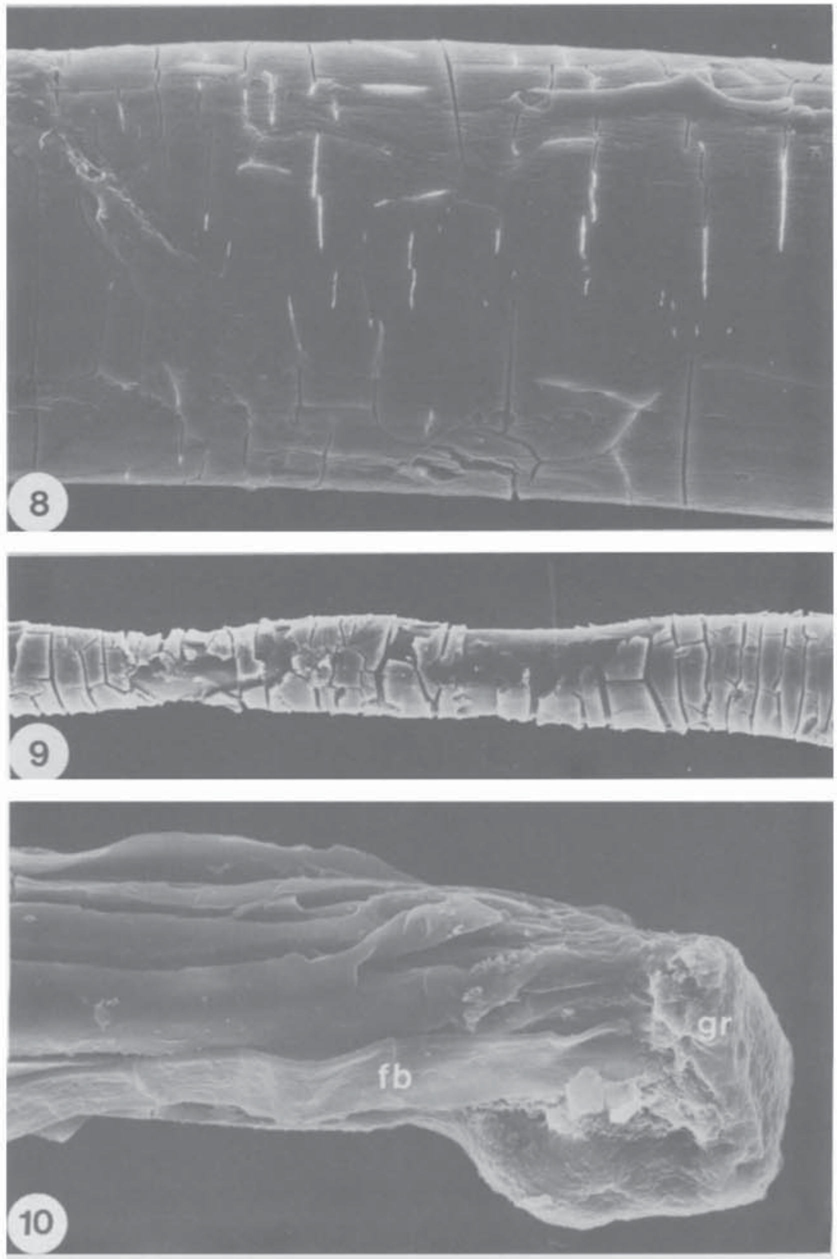


Figure 8. Central part of suture of Figure 1, which was not in contact with tissue. Some cracking of surface layer present; diameter 200 μm. Magn. 300 ×.

Figure 9. Part of right side of suture of Figure 1 at low magnification showing irregular diameter and cracking of surface layer. Magn. 120 ×.

Figure 10. Spontaneously broken end of suture of Figure 1 showing granular deposit (gr) and fibre-like material (fb) at the tip. Magn. 600 ×.

The spontaneously broken-off end of the suture, the actual reason for removal from the eye, is shown in Figure 10. The end of the surface is covered with slightly granular material and rather long strands of fibrillar material.

Figure 11 shows the destruction of the polypropylene in a rather dramatic way; the complete surface layer has broken into pieces, exposing the subsurface layer. The outside layer is covered with some deposits, mainly of a granular nature.

The subsurface layer is observable in more detail in Figure 12 (detail of Figure 11); the fibrillar character of this layer is clearly visible, while the splitting of the surface layer is noticeable, particularly at the cross-sections of the split-off lumps in the lower part of the picture.

The fibrillar character of the subsurface layer, and the irregular splitting of the surface layer from the underlying layer as the result of a chemical change in the surface layer, are shown in more detail in Figure 13.

In a virgin piece of surgical polypropylene, taken from an intact package, none of the phenomena described above are observable (Figure 14). The diameter is 200 μm and only thin grooves due to the manufacturing process are visible running along a very smooth surface (arrows).

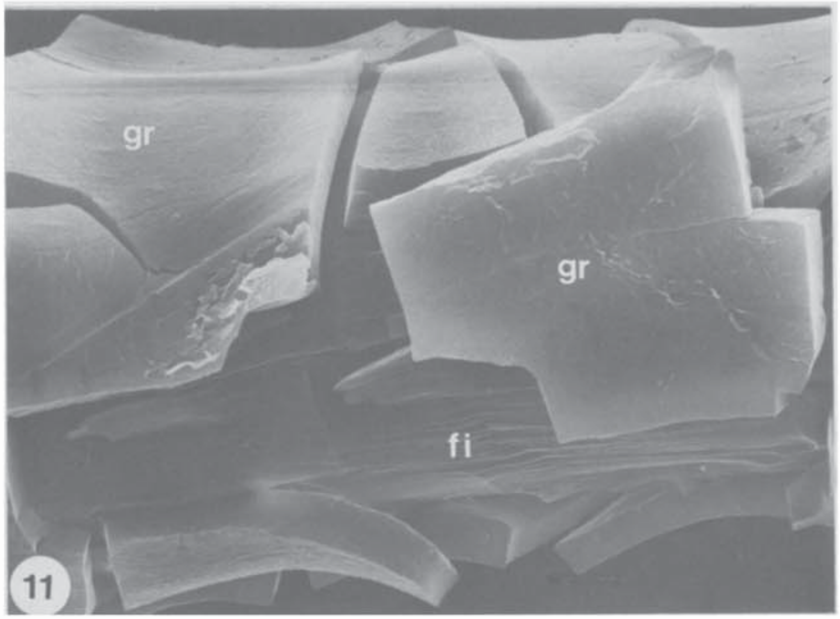
Discussion

Several investigators, Apple et al. (1984), Hessburg (1985), Drews (1983a, 1983b), Jongebloed et al. (1986) have reported changes in polypropylene material, used either as lens haptic or as suture material in the human eye for a period of at least 2 years. It is suggested by some observers that (bio)-degradation could be the cause of the phenomena observed (Apple et al. 1984; Jongebloed et al., 1986), while others are more inclined to think of artifacts caused by the preparation of the specimen for SEM.

In the opinion of those who think that the phenomena observed are merely an artifact, drying for the SEM, irradiation damage by the electron beam, or merely the drying of a deposited organic (protanaceous) layer, could be the cause.

The suture under investigation actually had an adhering layer, probably of organic nature. By careful washing in 50% ethanol this layer could easily be removed. The virgin polypropylene was washed in exactly the same way before drying in air. As can be seen from the pictures shown, a very thin coating of organic material remains on the used suture surface. This thin coating cannot contribute to the large scale degradation of the surface layer.

The drying procedure in air, which was exactly the same for the suture and the virgin material, cannot be the cause of the phenomena observed in this way, neither can the influence of the electron beam on the material. Otherwise we would have found changes in the virgin material as well.



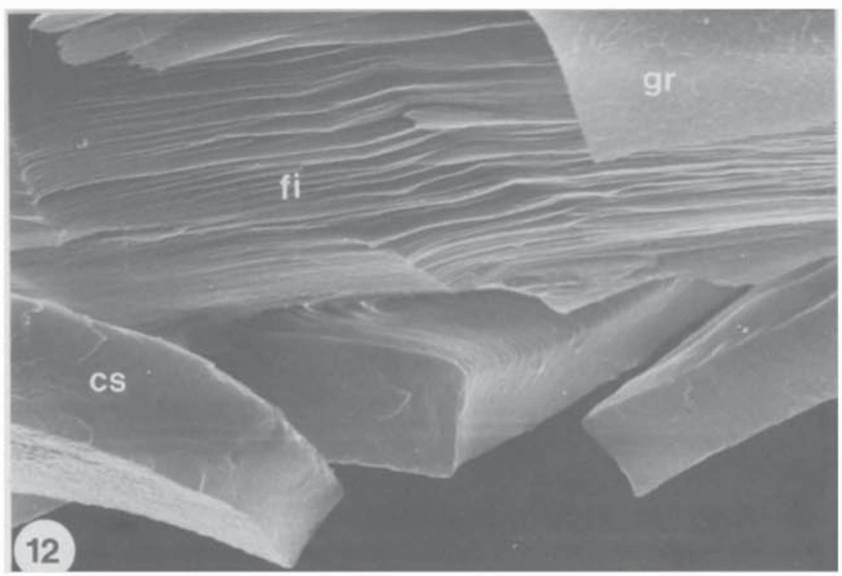
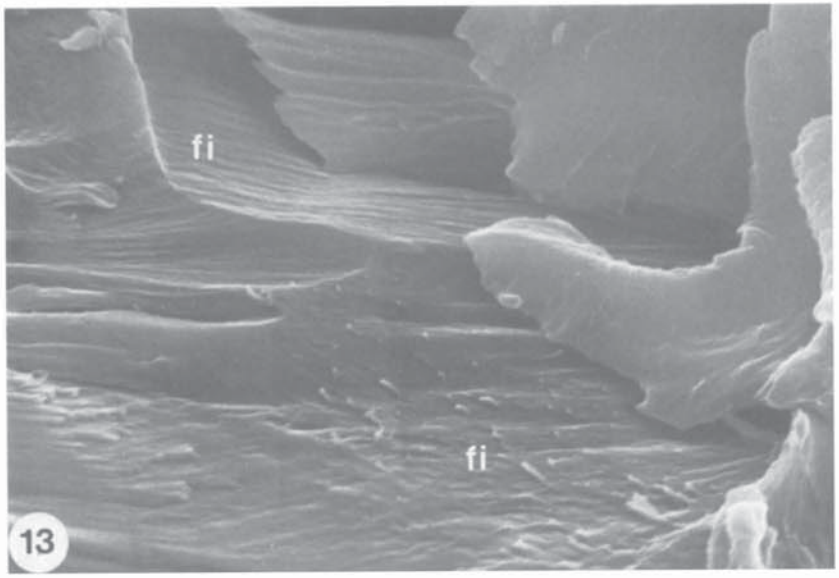


Figure 11. Part of right side of suture of Figure 1 showing almost complete degradation of surface layer, large lumps have detached exposing subsurface layer with fibrillar character (fi). Note granular deposit on lumps (gr). Magn. 975 ×.

Figure 12. Detail of Figure 11 showing subsurface layer (fi) and split-off lumps of surface layer in more detail (cs). Magn. 2500 ×.



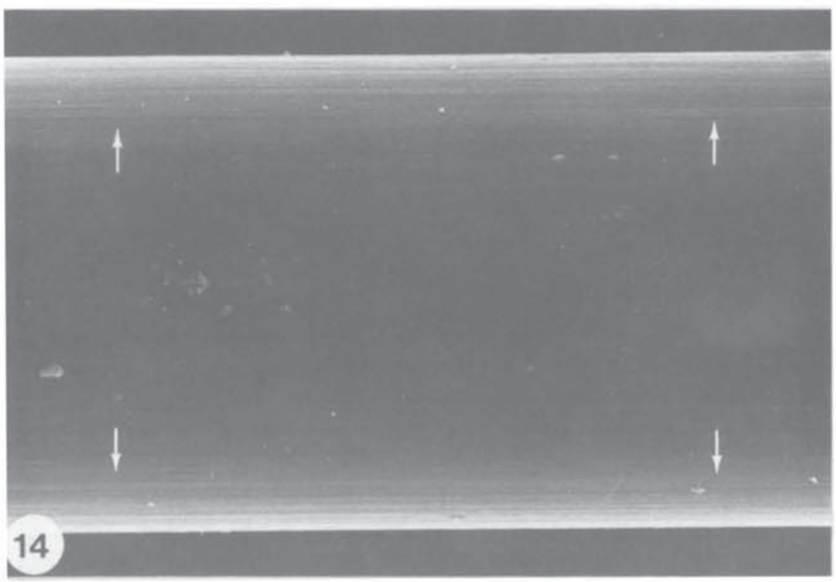


Figure 13. High magnification of subsurface layer after detachment of surface layer; note irregular splitting effect due to chemical change in polypropylene. Fibrillar character (fi) of subsurface layer clearly observable. Magn. 5000 ×.

Figure 14. Virgin piece of polypropylene from a surgical packet, prepared for SEM in exactly the same way as the suture of Figure 1, showing no degradation at all; note manufacturing grooves (arrows). Magn. 300 ×.

If the drying of a rather thick layer of adhering matter does not provide the explanation of the observed phenomena, what other options do we have?

Changes in the polypropylene are often associated with inflammatory conditions in the eye. This was not the case in our specimen. The failure of the IOL fixation suture was the primary reason for its removal. Inflammation of an eye and the presence of enzymes could be the primary cause of degradation of polypropylene. But because degradation also occurs in the absence of inflammation, as in our case, this cannot be the only cause.

The influence of UV-light and the role of sterilizing agents should not be overlooked and more research on these factors is certainly necessary. Whether f.e. sterilization in itself can provoke the phenomena described is nevertheless doubtful, because virgin sterilized material does not show any of the changes shown. The influence of UV-light can easily be studied in an in-vitro situation; this will be the subject of a future communication. It is more probable that if both UV-light and sterilizing agents contribute to the degradation of the polypropylene, they do so in the presence of enzymes. The assumption is, that the UV-light and the sterilizing agents make the polypropylene material more vulnerable to enzymatic attack. In our opinion the primary cause of the degradation should be attributed to the presence of enzymes, the more so because the severity of the degradation differs locally. In our case both ends of the fixation suture showed a substantial decrease in diameter, where they had been in direct contact with the tissues. Returning to the effects of drying, the drying certainly has enhanced the effects as shown. But it should not be forgotten that the suture had already broken at one side in the eye because it had become very thin there. The other end was quite thin as well, while the middle part of the suture, which was not in direct contact with the tissue, had retained its original diameter. Concluding, we might say that biodegradation is the primary cause of the phenomena observed, possibly enhanced by the influence of sterilizing agents and UV-light, which make the material more vulnerable to enzymatic attack.

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